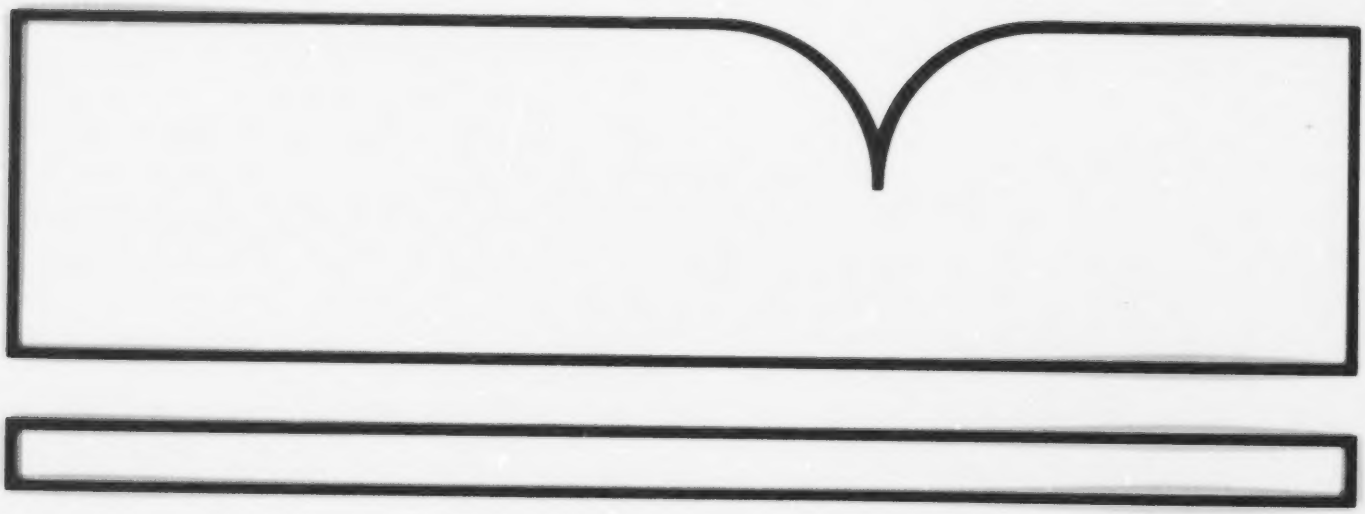
PB88-236831

Pesticide Fact Sheet Number 170
Maleic Hydrazide

(U.S.) Environmental Protection Agency
Washington, DC

30 Jun 88



U.S. Department of Commerce
National Technical Information Service
NTIS

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO.	2.	3. PB88-236631
4. Title and Subtitle EPA Pesticide Fact Sheets -Maleic Hydrazide No. 170			5. Report Date June 30, 1988 6.
7. Author(s) EPA, Office of Pesticide Programs, Registration Division			8. Performing Organization Rept. No. 540/FS-88-100
9. Performing Organization Name and Address U.S. Environmental Protection Agency Office of Pesticide Programs Registration Division (TS-767C) 401 M Street, SW Washington, D.C. 20460			10. Project/Task/Work Unit No. 11. Contract(C) or Grant(G) No. (C) (G)
12. Sponsoring Organization Name and Address Same as #9			13. Type of Report & Period Covered 14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA 22161

c. COSATI Field/Group

18. Availability Statement: Publicly Available	19. Security Class (This Report) Unclassified	21. No. of Pages 12
	20. Security Class (This Page) Unclassified	22. Price

United States
Environmental Protection
Agency

Office of Pesticides and Toxic Substances
Office of Pesticide Programs (TS-766C)
Washington, DC 20460

540/FS-88-100

EPA

Pesticide Fact Sheet

Name of Chemical: MALEIC HYDRAZIDE
Reason for Issuance: REGISTRATION STANDARD
Date Issued: JUNE 30, 1988
Fact Sheet Number: 170

1. Description of Chemical

Generic Name: 1,2-dihydro-3,6-pyridazinedione

Common Name: Maleic Hydrazide

Trade Names: Drexel Sucker-Stuff, Super Sucker Stuff, Retard, Burtolin, Decut, Drexel Sprout Stop, Fair 2, Fair Plus, KMH, Maintain 3, Malazide, Mazide, Regulox W, Regulox 50W, Stuntman, Super-De-Sprout, Vendalhyde, Vondrax, Royal MH-30, Royal MH-30 SG, Royal Slo-Gro, Malazide Slo Gro.

EPA Shaughnessy Codes: Maleic Hydrazide: 051501
Potassium Salt of Maleic Hydrazide: 051503
Diethanolamine Salt of Maleic Hydrazide: 051502

Chemical Abstracts Service (CAS) Number: 123-33-1

Year of Initial Registration: 1952

Pesticide Type: Herbicide, Plant Growth Regulator

U. S. and Foreign Producers: Drexel Chemical
Trans Chemical Industries
Uniroyal Chemical, Inc.

2. Use Patterns and Formulations:

Application Sites: Terrestrial food (potatoes, onions, cranberries), terrestrial nonfood (nonbearing citrus and nonbearing apples, tobacco), terrestrial noncrop.

Types and Methods of Application: Primarily as a foliar spray with some use by tree injection.

Pests Controlled: Sucker control for tobacco, sprout infiltration in onions and potatoes, growth retardant of quackgrass, wild onions, and garlic.

Application Rates:
Terrestrial Food Crops: 0.7 lb acid equivalent (ae)/A to 15 lb ae/A
Terrestrial Nonfood Crops: 1.5 to 4.5 lb ae/A
Ornamental Plants and Forest Trees: 0.06 to 6 lb ae/A
Turf: 0.75 to 6.6 lb ae/A
Rights-of-Way: 0.66 to 6.6 lb ae/A

Types of Formulation:
90%, 95%, 97%, and 99% technical grade of the active ingredient (TGAI)
0.66 to 2.25 lb ae/gal emulsifiable concentrate (EC)
0.6, 1.5, 2.0, 2.25, and 2.5 ae/gal soluble concentrate/liquid (SC/L)

Usual Carrier: Water

3. Science Findings

Summary Science Statement: Maleic hydrazide (MH) has low acute toxicity (Category III) for primary eye irritation and is in Category IV for acute oral toxicity, acute dermal toxicity, and primary dermal irritation. MH caused no adverse reproductive effects and was not oncogenic in mice. The teratology study in rabbits had a teratogenic NOEL of 100 mg/kg with malformed scapulae occurring in the mid and high dose. Additional information has been requested to clarify this effect.

MH was stable to hydrolysis and photodegradation in soil. It photodegraded in buffered aqueous solutions at pH 5, 7, and 9. MH was very mobile in five soils and has a low potential to bioaccumulate in fish. Additional persistence and leaching data are needed to evaluate MH potential to contaminate ground water.

MH is considered practically nontoxic to birds, aquatic invertebrates, freshwater fish, or honey bees. Endangered animal species are not expected to be adversely affected by the use of MH. Since no endangered plant species are listed for tobacco cropland, citrus, apples, or cropland with onions, potatoes, or cranberries, little risk to endangered plants is expected from these uses. The hazard evaluation for listed plants and the right-of-way uses is being deferred until completion of the noncrops cluster.

Chemical Characteristics:
Color: White
Physical state: Crystalline solid

Odor: Faint
Melting point: 292 °C minimum
Bulk density: 30 to 36 lbs cubic feet (cu/ft)
(0.049 grams/milliliter g/ml)

Specific gravity: 1.6 at 20 °C

Solubility:
90% a.e.- 60 parts per million (ppm) water
10 ppm isopropyl alcohol
< 10 ppm xylene
240 ppm dimethyl formamide

Vapor pressure: < 1 mm Hg at 20 °C

Stability:
Stable at 45 °C up to 61 days
Stable at 80 °C up to 30 days

Toxicology Characteristics:
Existing data are all based on MH (technical) or the potassium salt (K salt), further data are requested on the diethanolamine (DEA) salt.

Acute Toxicology:
Acute Oral Toxicity (Rat):
Greater than (>) 5 grams/kilogram (g/kg)
Toxicity Category IV
Acute Dermal Toxicity (Rabbit):
> 20 g/kg
Toxicity Category IV
Primary Eye Irritation:
Primary Irritation Score (PIS) = 0.4
Toxicity Category III
Primary Dermal Irritation:
Slight Irritant
Toxicity Category IV
Acute Inhalation and dermal sensitization studies are not available and are being required for MH and the DEA salt.

Subchronic Toxicology Studies: There are no data available for subchronic oral, dermal, or inhalation toxicity. A 21-day dermal toxicity study is required for both MH (technical MH or potassium (K) salt are considered equivalent) and the diethanolamine (DEA) salt. Subchronic feeding studies for a rodent and nonrodent are not required because chronic feeding studies are required.

Chronic Feeding/Oncogenicity Studies: Available chronic feeding studies are inadequate to fulfill guideline requirements but are useful to calculate provisional allowable daily intake (PADI). The chronic feeding study in rats indicates that the no-observable-effect level (NOEL) is less than (<) 500 milligrams/kilogram (mg/kg). Chronic feeding studies on rodents and nonrodents are required for both MH and its DEA salt.

Available oncogenic studies in rats are inadequate for maleic hydrazide technical and K salt, no data are available for the DEA salt, therefore data are required for both technical and DEA salt. Two oncogenicity studies are available for mice. Together they indicate that MH is not oncogenic in mice up to 1800 mg/kg. An oncogenic study in mice is required for the DEA salt.

Teratology and Reproduction Studies: A teratogenicity study in rabbits showed that exposure to 300 or 1000 mg/kg resulted in malformed scapulae in offspring, while 100 mg/kg had no effects. Additional information is required on parentage of affected offspring to fully evaluate this effect.

No teratology data are available for rats. Therefore, teratology studies are required for both MH and its DEA salt. A teratology study in rabbits is required for the DEA salt.

A 2-generation rat reproduction study indicated no incidence of adverse reproductive effects up to 2250 mg/kg (highest dose tested [HDT]) with fetal toxic and maternal toxic NOEL of 750 mg/kg based on decreased body weights at the HDT. This study satisfies the requirement for the MH technical. A 2-generation reproduction study in rats is required for the DEA salt.

Mutagenicity Studies: A mutagenicity study of sex-linked recessive lethal gene mutations in Drosophila revealed no sex-linked recessive lethal mutations at cytotoxic doses of 0.4 to 1.0% K salt of MH. All other mutagenicity data are required for MH. A full set of mutagenicity studies for the DEA salt are required.

Metabolism Studies: There are no metabolism studies available for MH technical or the DEA salt; therefore, these studies are required.

Physiological and Behavioral Characteristics:

Foliar Absorption - Absorbed by roots and leaves.

Translocation - Rapidly translocated to leaves and growing shoots.

Mechanism of Pesticidal Action - A uracil antimetabolite which interferes with cell division, plant growth, and maturation.

Metabolism in Plants - Limited available data indicate that the major residues in tobacco are maleic hydrazide and its beta-D-glucoside conjugate. Additional plant metabolism data are required for potatoes, onions and cranberries.

Metabolism in Animals - No data are available for metabolism in animals; therefore, livestock metabolism data is required.

Environmental Characteristics:

Adsorption and Leaching in Basic Soil Types: MH was very mobile in a silt loam, a sandy clay loam, a sandy loam, and two sandy soils. Additional leaching and adsorption data are required.

Microbial Breakdown: Available aerobic/anaerobic soil metabolism data are insufficient. Therefore, aerobic and anaerobic soil metabolism studies are required.

Loss from Photodecomposition: Stable to photodegradation in soil. Photodegraded in buffered aqueous solutions at pH 5,and 7,and 9 with half-lives of 58 days, at ph 5 and 7 and 34 days at pH 9.

Bioaccumulation: Low potential to bioaccumulate in fish.

Potential to Contaminate Ground Water: The available data are inconclusive for defining potential of MH to leach into ground water. MH is persistent in water. Once persistence data from aerobic/anaerobic soil metabolism data and additional leaching data are submitted, the potential to contaminate ground water will be evaluated.

Exposure to Humans: Humans may be exposed to maleic Hydrazide by ingestion of residues on treated crops, and from use of treated tobacco. The major route of exposure for applicators is expected to be dermal contact. An exposure assessment was performed for application on tobacco, potatoes, onions, and rights-of-way. Exposure ranged from less than 0.5 mg/kg/day to 16 mg/kg/day. The greatest exposure occurred for the open-pour mixer loader.

Risk to Humans: The major routes of exposures are expected to be dermal and eye contact. A risk assessment was performed for dermal exposure to applicators based on a rare teratogenic effect (malformed scapulae in offspring) seen in rabbits. The risk assessment indicated that the margin of safety (MOS) for mixer-loaders was less than 100 and therefore of concern. Labels for end-use products (EPs) are being amended to require long sleeve shirts, long pants, chemical resistant gloves at all times while handling, applying, mixing, or loading the product.

Reentry: Reentry data are not required at this time because cultural practices for existing uses indicate little likelihood of exposure or low exposure from these uses. Because MH is placed in Toxicity Category IV for acute oral and dermal toxicity, minimal risk to humans is expected.

Ecological Characteristics:

Avian Acute Adult Toxicity:
Technical: Mallard Duck > 4640 mg/kg
K salt: Mallard Duck > 2250 mg/kg

Avian Dietary Toxicity:
Technical:
Mallard Duck > 10,000 ppm
Bobwhite Quail > 10,000 ppm
K salt: Mallard Duck > 5620 ppm

Acute Toxicity to Freshwater Fish:
Technical:
Rainbow Trout = 1435 ppm
Bluegill = 1608 ppm
K salt: Rainbow Trout > 1000 ppm

Acute Toxicity to Freshwater Invertebrates:
Technical: 107.5 ppm
K salt: 1000 ppm

Acute Toxicity to Honey Bee: > 36.26 ug/bee

These data indicate that MH is considered "very low toxicity" to avian species, both warmwater and coldwater fish, freshwater invertebrates, and honey bees.

Hazard to Endangered Species: Endangered animal species are not expected to be adversely affected by the use of MH because of its low toxicity to mammals, avian species, and aquatic species.

Since MH is a plant growth retardant endangered plant species occurring in areas where MH is used could be at risk. However, there are no endangered plant species listed for tobacco cropland, citrus, apples, or cropland planted with potatoes, onions, or cranberries, therefore no risk to endangered plant species. Evaluation of hazard to indangered plants from use of MH on right-of-way will await completion of noncrop cluster.

Tolerance Assessment: Tolerances are established in 40 CFR 180.175 for residues of the herbicide and plant growth regulator MH (1,2-dihydro-3,6-pyridazinedione) in or on the following raw agricultural commodities:

Commodity	Parts per million
Cranberries	15.0
Onions, dry bulb	15.0
Potatoes	50.0

A tolerance is established in 21 CFR 193.270 for residues of the herbicide and plant growth regulator (1,2-dihydro-3,6-pyridazine-dione) on potato chips at 160 ppm as a result of application of the pesticide to the growing potato plant.

A Provisional Acceptable Daily Intake (PADI) for MH is currently based on the finding of renal dysfunction in the rat chronic study. The LOEL for this effect was 500 mg/kg/ day. Using a thousandfold safety factor, the PADI for MH is 0.5 mg/kg/day. Existing tolerances produce a theoretical maximum residue contribution (TMRC) of 0.085 mg/kg/day which occupies 17 percent of the PADI.

The tolerance assessment indicated that additional residue data are needed for onions, potatoes, nonbearing apples, and nonbearing citrus. Additional plant metabolism data are required for MH. No storage stability or animal metabolism data are available; therefore, these data are required.

Available toxicology data that was used to calculate the PADI on technical or K salt include oncogenicity studies in mice, a teratology study in rabbits, and a 2-generation rat reproduction study. Additional data required include chronic feeding studies with a rodent (although the PADI was established based on a supplementary feeding study in rats) and nonrodent oncogenenicity and teratology studies in rats, mutagenicity testing, and rat metabolism data for the technical or K salt. Data required to support tolerances for the DEA salt include acute data, chronic feeding studies with a rodent, non-rodent, oncongenicity studies in rats and mice, teratology studies with rats and rabbits 2-generation rat reproduction study, mutagenicity testing and metabolism data.

Reported Pesticide Incidents

Data from the Pesticide Incident Monitoring System (PIMS) reports and the national study of hospitalized pesticide poisonings (1971-76) show some cases of MH poisonings, mostly occupational. There were an estimated eight persons hospitalized in the United States each year from 1974 to 1976. The circumstances that led to these poisonings are not known.

4. Summary of Regulatory Position and Rationale

A review of the available data indicate that no risk critera listed in 40 CFR 154.7 have been met or exceeded for MH.

The Agency will not approve any significant new uses of MH until additional residue chemistry data are available to assess existing uses.

The Agency is requiring that labeling on all EPs include a requirement for protective clothing long-sleeve shirt, long pants and chemical resistant gloves at all times when handing, applying, mixing, or loading pesticide.

Products bearing labelling not in compliance with the registration Standard may be released for shipment by the registrant only until July 30, 1989. Such products may be distributed and sold by other persons only until July 30 1990.

The Agency is requiring that additional leaching, aerobic/ anaerobic soil metabolism and dissipation data be submitted to fully define the MH potential to leach and contaminate groundwater.

The Agency is requiring that additional information be submitted on the rabbit teratology study and that a rat teratology be completed within twelve (12) months.

The Agency will continue to require that the acceptable limit of hydrazine occurring in technical products be $\leq$ 15ppm as required by the PD-4

The Agency has determined that all toxicology studies will be necessary for the diethanolamine salt of maleic hydrazide if manufacturers comply with the data requirements which resulted in the suspension of all DEA-MH products in November 1981.

The Agency has determined that all end use product chemistry data for technical MH must be resubmitted and updated.

The Agency has determined that all products containing the DEA salt must be tested for nitrosamines.

The Agency has determined that reentry data or restrictions are not required at this time.

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The Agency will not require labeling to protect endangered species at this time for products containing maleic hydrazide.

The Agency has determined that Tier I nontarget area phytotoxicity testing will be required for MH.

The Agency will not require additional residue data on cranberries.

The Agency will require additional residue data on potatoes, onions, tobacco, nonbearing citrus, and nonbearing apples.

The Agency is requiring additional animal and plant metabolism data and storage stability data on all residue data previously submitted and any new residue data requested.

The Agency has determined that certain data essential to the Agency's assessment of this pesticide and its uses and/or that may trigger the need for further data will receive immediate review when submitted. These data include animal and plant metabolism data, data necessary to determine the MH potential to contaminate ground water, and all requested toxicology data.

5. Summary of Major Data Gaps

Requirements	Due Dates
Product Chemistry	6 to 15 months
Residue Data	6 to 24 months
Toxicology Data	9 to 50 months
Environmental Fate	9 to 39 months
Plant Protection	9 months

6. Contact Person at EPA:

Robert J. Taylor (PM 25)
Fungicide-Herbicide Branch
Registration Division (TS-767C)
Environmental Protection Agency
401 M Street SW.
Washington, D.C. 20460
(703) 557-1800

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